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TRIMETHOPRIM-SULPHAMETHOXAZOLE IN ACUTE BRUCELLOSIS

By

A. Hassan, M.M. Erian, Z. Farid
S.D. Hathout, K. Sorensen

U. S. NAVAL MEDICAL RESEARCH UNIT No.3
(CAIRO, THE ARAB REPUBLIC OF EGYPT)
FPO NEW YORK 09527

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A. Hassan, M.M. Erian, Z. Farid, S.E. Hathout, K. Sorensen

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Eight patients with proved brucella infection were treated with trimethoprim-sulphamethoxazole. The dose varied from two to four tablets given twice daily for three weeks. Clinical response was rapid and all patients were asymptomatic and afebrile within two to seven days of starting therapy. Three patients relapsed clinically and bacteriologically within three weeks of ending treatment. It is suggested that the treatment be continued for at least six weeks to prevent relapses.

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Trimethoprim-sulphamethoxazole in Acute Brucellosis

A. HASSAN, M. M. ERIAN, Z. FARID,
S. D. HATHOUT, K. SORENSEN

Summary

Eight patients with proved brucella infection were treated with trimethoprim-sulphamethoxazole. The dose varied from two to four tablets given twice daily for three weeks. Clinical response was rapid and all patients were asymptomatic and afebrile within two to seven days of starting therapy. Three patients relapsed clinically and bacteriologically within three weeks of ending treatment. There were no side effects of the treatment. It is suggested that the treatment be continued for at least six weeks to prevent relapses.

Introduction

We (Farid *et al.*, 1970) noted the remarkable effectiveness of trimethoprim-sulphamethoxazole (Septrin, Bactrim) in the treatment of acute typhoid and paratyphoid fevers and also in

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Abbassia Fever Hospital, Ministry of Public Health, Cairo, Egypt
ANWAR HASSAN, D.M., Director
M. M. ERIAN, M.B., Registrar
S. D. HATHOUT, D.M., Assistant Director

U.S. Naval Medical Research Unit No. 3, Cairo, Egypt
Z. FARID, M.D., D.T.M.&H., Head of Tropical Medicine Department
K. SORENSEN, M.D., Head of Medical Department

two patients with proved brucella septicaemia. Simultaneously Lal *et al.* (1970), from the United Kingdom, reported the successful use of this treatment in three out of four patients with acute brucellosis and emphasized that their patients were asymptomatic and afebrile within 24 to 48 hours of starting treatment. We report here on the treatment of an additional eight patients with acute *Brucella melitensis* infection with trimethoprim-sulphamethoxazole.

Patients and Methods

Six out of the eight patients treated belonged to one family—father, mother, three sons, and one daughter—the seventh patient was the brother of the father. All lived in Cairo, owned goats and cattle, and drank raw milk. They fell ill at about the same time during the period December 1970 to February 1971. The eighth patient was a farmer from a village near Cairo. The eight patients, six males and two females, were aged 8 to 62 years. All were acutely ill and complained of an afternoon rise of temperature accompanied by profuse sweating, with muscle and joint aches and pains. The family of six and the brother gave a short history of one to four weeks of illness; the farmer gave a history of recurrent febrile attacks for eight weeks. All had raised brucella tube agglutination titres and positive blood cultures for *Br. melitensis.*

Blood cultures were made on double-phase Castaneda (1947) bottles. Treatment was standardized at a dose of 10 mg of trimethoprim and 50 mg of sulphamethoxazole per kg per day. (Each tablet contains trimethoprim 80 mg and sulphamethoxazole 400 mg; a ratio of 1 to 5.) The total daily dose was divided into two portions given 12 hours apart. Treatment was given for three weeks. The youngest patient received two tablets twice daily and the older men received up to four tablets twice daily. All were kept in hospital for at least four weeks after completing treatment and were then followed up as outpatients for as long as possible.

Results

The results are summarized in the Table. All patients were asymptomatic within two to four days of starting treatment; headache, profuse sweating, myalgia, and arthralgia were rapidly relieved. The return of temperature to normal was somewhat slower and took from two to seven days. All patients tolerated medication very well and there were no side effects.

Treatment of Acute Brucellosis with Trimethoprim-Sulphamethoxazole

Patients	Age (Years)	Weeks Ill before Treatment	Maximum Temperature before Treatment	No. of Days to become Asymptomatic	No. of Days to become Afebrile	Comments
Father	45	3	39°C	3	4	Uneventful recovery, followed up for 3 months
Mother ..	35	4	38°C	4	6	Uneventful recovery, followed up for 3 months
Elder son ..	17	2	39°C	3	5	Treatment extended to 6 weeks,* recovery complete, follow-up 1 month
Middle son ..	15	2	39°C	4	7	Febrile and symptomatic 3 weeks after treatment. Blood cultures positive. Prompt response to retreatment for 6 weeks, with full *recovery; followed up for 1 month*
Younger son ..	12	1	39°C	2	2	Blood cultures positive 1 week after treatment. Febrile and arthritis of right elbow 4 weeks later. Prompt response to retreatment for 6 weeks, with full recovery; 1 month follow-up
Daughter ..	8	1	39°C	3	3	Uneventful recovery, followed up for 3 months
Brother ..	47	4	38°C	2	3	Treatment extended to 6 weeks,* with full recovery; follow-up 1 month
Farmer ..	62	8	39°C	4	2	Blood cultures positive 1 week after treatment. Severe low backache and febrile 1 week later. Re-treated with tetracycline and streptomycin
Female† ..	11	3	40°C	3	4	Both patients followed up for 12 months. Agglutination titres and repeated blood cultures *remained negative*
Female† ..	16	48	40°C	4	5	

*After the three relapses it was decided to extend treatment in further patients to a minimum of 6 weeks.

†Treated in 1970 (Farid *et al.*, 1970).

Three patients (the middle son, younger son, and the farmer) relapsed one to three weeks after ending treatment; all became symptomatic and had positive blood cultures for *Br. melitensis*. The farmer was re-treated with tetracycline and streptomycin because of suspected brucella spondylitis (Farid and Omar, 1965). The middle and younger sons were successfully re-treated with trimethoprim-sulphamethoxazole, but this time the course of treatment was extended to six weeks.

Discussion

There is little doubt that trimethoprim-sulphamethoxazole rapidly controls the acute symptoms of brucellosis. This has been our experience in the treatment of a total of 10 acutely ill patients with proved brucella septicaemia. All became asymptomatic and afebrile within two to seven days of starting treatment. Three patients, however, relapsed a few weeks after completing therapy. Relapses after treatment have always been a recurrent problem in the treatment of acute brucellosis with any of the broad-spectrum antibiotics, and we (Farid *et al.*, 1961, 1963) and others from Egypt (Killough *et al.*, 1951; Magill and Killough, 1953; Pfischner *et al.*, 1957) have reported relapse rates of 14 to 70% with different antibiotic regimens.

At present the standard treatment recommended for acute brucellosis is prolonged and repeated courses of tetracycline with the addition of intramuscular streptomycin. Treatment with trimethoprim-sulphamethoxazole is simpler and causes less discomfort to the patient. More prolonged treatment, however—and we suggest at least six weeks or repeated courses of therapy—will definitely be necessary to reduce the relapse rate. The complete absence of side effects with trimethoprim-sulphamethoxazole makes such long or repeated courses possible. Whether this will be an advantage over combined tetracycline and streptomycin remains to be seen.

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